ANNUAL REPORT

OF

THE HOWE LABORATORY
OF
OPHTHALMOLOGY
HARVARD MEDICAL SCHOOL
AT THE
MASSACHUSETTS EYE AND EAR INFIRMARY

1967

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Special Fellowships:

Mario V. Aquino, M.D.: *USPHS (Center Grant)*
William M. Haining, M.D.: *E. B. Dunphy Fellowship and USPHS (Center Grant)*
Shirley H. Wray, M.D.: *USPHS (Center Grant)*
Philip H. Zweifach, M.D.: *USPHS (Center Grant)*

Residents of the Massachusetts Eye and Ear Infirmary

Richard F. Brubaker, M.D.
Leo T. Chylack, Jr., M.D.
William J. Collis, M.D.
Steven V. Guzak, M.D.
Gordon J. Johnson, M.D.
Brent W. Lambert, M.D.
Deborah P. Langston, M.D.
Joseph Michon, Jr., M.D.
Anthony B. Nesburn, M.D.
Ronald C. Pruett, M.D.
Richard A. Thoft, M.D.
David M. Worthen, M.D.

Predoctoral Students

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Researches in the Howe Laboratory in 1967 included many and varied projects having in common the eye as a center of interest. A list would have to include the study of glaucoma, cataracts, enzyme kinetics, identification of ultrastructural organelles, development of new instruments, recognition of potential poisons, evaluation of drugs, and multitudinous other activities. Some yielded fruitful results; many did not.

This Report is a partial account of these researches emphasizing their aims and relationships with allied activities. The essential factor in all is, of course, the investigator. But the investigator's environment may also play a determinant role in his orientation and productivity. The aim of the Howe Laboratory is to provide an environment which, to the limit of our space and resources, is favorable for those with talents for research on the eye and its diseases. In this we have the tremendous help of many friends who may have only tangential contact with the Laboratory but who have expressed their confidence in its aims by assistance in multiple ways.

RESEARCH ACTIVITIES

Glaucoma

Research relating to glaucoma is carried on by postgraduate research fellows, by residents and by pre-residency N. I. H. trainees, generally in consultation with Dr. Grant whether carried on within the Howe Laboratory or the Glaucoma Consultation Service or elsewhere within the Infirmary. This Report will encompass all these activities.

Testing and evaluation of drugs

One portion of glaucoma research has been concerned with clinical testing and evaluation of drugs. Some of the drugs were tested with the expectation that they might help in treating glaucoma or might yield information fundamental to understanding glaucoma. Other drugs have been tested because of apprehensions that they might constitute a hazard in glaucoma. Our activity in this particular type of investigation reflects a world-wide increase in studies of medical treatment of glaucoma, encouraged in recent years by several useful discoveries, and it reflects the new official attention of the Food and Drug Administration to efficacy and hazards of drugs. This brings together Dr. Grant's principal interests, which are in glaucoma and in toxicology and pharmacology of the eye. Dr. Grant has been participating in the activities of the National Research Council, the U. S. Pharmacopeia, The National Institutes of Health and the Drug Committee of the American Academy of Ophthalmology and Otolaryngology in organizing and appraising information in these fields.

The clinical studies on drugs in glaucoma have been carried out principally by Dr. Peczon. In previous years Dr. Peczon has published evaluations of sedatives and stimulants, digitalis, methyldopa, corticosteroids and other types of drugs, and he has dispelled the common belief that alcoholic beverages might be harmful for glaucoma, showing instead that alcohol could transiently reduce ocular pressure. This year Dr. Peczon's attention was temporarily diverted to a study of the effects of the common aspirin when fortuitously one patient appeared to have a considerable fall of pressure after taking aspirin, but repeated trials in a number of glaucomatous patients failed to establish any consistent influence on ocular pressure.

Dr. Peczon this year has carried out a systematic evaluation of several different types of diuretic drugs in glaucomatous patients. This was prompted by the knowledge that ocular pressure in glaucoma is reduced by one category of diuretic drugs, the carbonic anhydrase inhibitors such as Diamox, and by substances such as alcohol and mannitol that induce diuresis either by suppression of antidiuretic hormone or by osmotic action. Dr. Peczon tested several diuretics differing chemically and in mechanism of action on the kidney, looking for an influence on formation or outflow of aqueous humor that would alter intraocular pressure. These diuretics could conceivably lower the intraocular pressure, which would be beneficial in glaucoma, or raise it, which would be hazardous to glaucomatous patients if by chance they also had other disease for which they were given the drug without thought of their glaucoma. As the studies turned out, these drugs were found not to have adverse effect on ocular pressure, but unfortunately neither did they have clinically worthwhile ocular pressure reducing effect. From this was learned that diuresis itself does not reduce ocular pressure unless the kidney is made to excrete urine which is hypotonic compared to the blood, an effect apparently not achieved by these drugs. Also this study gave added support to the belief that the carbonic anhydrase inhibiting drugs such as Diamox reduce the ocular pressure by interfering with formation of aqueous humor by a highly specific action directly in the eye and not dependent upon diuresis.

Dr. Peczon, recently with the help of Dr. Aquino, has also been evaluating the influence of systemic vasodilator drugs in glaucoma. These drugs have various medical uses. Some are used to relieve symptoms of coronary heart disease and some are intended for improvement of circulation in the brain and in the legs and arms. There has been uncertainty and apprehension concerning possible adverse influence of these drugs on the ocular pressure in glaucoma, but practically no evidence. The apprehensions have been partly based on ideas on the pathogenesis of glaucoma prevalent more than half a century ago but greatly changed in modern times, and partly based on demonstrations that strong vasodilators injected directly into the tissues about the eye can cause a transient small rise in ocular pressure greater in glaucomatous than in normal eyes. On the other hand, there are a number of reports of systemic vasodilators having been given to glaucomatous patients, without regard to the pressure, with the intent of improving circulation of the optic nerve and retina, and several claims of improvement of vision have been made. To help clarify the situation, Dr. Peczon had previously worked with Dr. Whitworth in establishing that nitrate and nitrite vasodilators such as used in coronary disease had no adverse effect in glaucomatous eyes or eyes with pathologically narrowed angles. Now he has been determining whether the other types of vasodilators, including nicotinic acid and cyclandelate, are safe for use by glaucomatous patients not only for treatment of peripheral vascular disease, but also for more careful evaluation of claims of benefit to vision. So far the evidence indicates little or no danger.

Drs. Lazenby and Reed have been examining the safety of another group of systemic drugs, the anticholinergic or atropine-like medicines. More than 50 medications having anticholinergic properties are sold and used variously to treat gastrointestinal spasm and ulcers, to relieve Parkinsonism, to alleviate hayfever and other allergies, and to treat mental illness. The likelihood is strong that some of these may be taken by patients who have glaucoma or are prone to develop glaucoma, and there are grounds for apprehension that these medications might make the ocular pressure rise. The apprehension is based primarily on knowledge that anticholinergic drugs when applied directly to the eye can in certain cases induce acute angle-closure glaucoma by causing the pupil to dilate, and can make the pressure rise in open-angle glaucoma by paralyzing the ciliary muscle. However, apart from isolated instances of acute glaucoma from systemic administration of atropine, there is little factual information on the influence of the anticholinergic drugs when given systemically. Their effects need to be investigated with respect to two different types of glaucoma (acute angle-closure and chronic open-angle). The chronic open-angle type has been selected for investigations of the effects of anticholinergic drugs because this type is much more prevalent in this country, the patient usually has it for many years during which the chance of encountering anticholinergic medications is great, and the influence on the control of the glaucoma can be directly evaluated, whereas the angle-closure type of glaucoma is less common, less predictable, occurs suddenly and requires prompt surgery rather than prolonged treatment and observation.

Use has been made of the fact that patients with chronic open-angle glaucoma in the course of their regular treatment periodically have their pupils dilated with anticholinergic eye drops to permit proper examination of their optic nerves and visual fields. Elevation of ocular pressure occurs transiently during this necessary examination procedure, more in some patients than in others, though the angles remain clearly open in all. Presumably those patients with the greatest rise of pressure from the application of anticholinergic drugs to the eye would be the ones most likely to have adverse effect if they encountered one of the many anticholinergic medications that are given orally. In fact, according to their histories some of the patients in the past had taken such medications without knowledge of possible influence on glaucoma. Those patients who understood the potential significance of these observations have been studied with and without oral anticholinergic drugs under closely controlled conditions, with and without their regular antiglaucoma medications. The results so far have been fortunately reassuring, suggesting that when open-angle glaucoma is under regular treatment the taking of anticholinergic drugs orally is satisfactorily tolerated. Long-term observations and studies in relation to angle-closure glaucoma are still needed.

Glaucoma in childhood

Glaucoma in childhood is rare compared to the approximate incidence of one to two per hundred in older people, but it is nevertheless important because if not recognized and treated early it is blinding, whereas early goniotomy operation in a large proportion of cases is successful. Efforts are continuously being made to improve surgical techniques and to recognize and distinguish the special characteristics of different types of glaucoma that occur in childhood. This year Dr. Amoils while a Research Fellow has devised a special knife for goniotomy, carrying its own light source into the eye by means of a flexible fiber optic bundle, probably better overcoming some of the special problems presented by corneal haze that last year was only partially alleviated by Dr. Grant's introduction of a miniature, sterile, prefocused light held close to the site of surgery. Dr. Amoils has since been supported by glaucoma funds to carry out further clinical evaluation and development work on this in association with Dr. Simmons. Dr. Amoils is also evaluating the effects of very low temperature freezing of the ciliary body in treatment of glaucoma in certain types of patients.

Drs. Walton and Grant have made a clinical study of one of the rarest causes of glaucoma in childhood, known as von Recklinhausen's disease or neurofibromatosis, and have been able to correlate the abnormalities in the angle with the pathogenesis of the glaucoma.

Neovascular glaucoma

A form of glaucoma caused by an abnormal growth of blood vessels and fibrous tissue blocking the outflow channels in the angle of the anterior chamber, known as neovascular or hemorrhagic glaucoma, is one of the most mysterious as to cause and one of the most difficult to treat. It is a well known and usually disastrous complication associated with diseases of retinal blood vessels, particularly common in association with advanced diabetes. Drs. Thoft and Peczon have been carrying on systematic clinical observations on the natural course of its development, which previously had not been adequately studied. Dr. Walton has established through systematic microscopic examination of eyes of children which have been removed with various blinding conditions that malignant retinoblastoma is the predominant cause of neovascularization of the iris and angle in children, providing another clue to the mystery of the mechanism.

Treatment of neovascular glaucoma surgically has proved discouraging, though Dr. Meyer and Dr. Niffenegger have succeeded in improving techniques of trephining surgery to overcome some of the problems and obtain prolonged relief of pressure. Unfortunately, especially in diabetic patients, relief of the pressure has not prevented blinding intraocular hemorrhages.

Another variety of filtering operation suggested by Dr. Chandler has been undergoing extensive clinical trials under supervision of Dr. Grant in desperate cases of glaucoma of several types including the neovascular and certain childhood glaucomas. This consists of making three or four holes through the sclera and posterior portion of the ciliary body with electric diathermy in a manner intended to allow drainage of fluid from the eye by this route, avoiding the iris and anterior chamber. This has been at least temporarily successful in some cases, but the proportion and duration of successes remain to be determined.

Pseudofacility and transport

In experimental work in monkeys Dr. Brubaker has studied pseudofacility of aqueous outflow by a new method consisting of maintaining the intraocular pressure by constant pressure infusion while varying the episcleral venous pressure by means of a cervical pressure cuff. Also Drs. Brubaker and Worthen have made experimental trials of vein transplants connected to a trephine opening in monkey eyes for the purpose of achieving filtration from the anterior chamber. They are now evaluating the results.

Dr. Worthen has been attempting to determine whether there are sites of selective uptake and transport of iodide in the ciliary body. He has attempted this in rabbits using radio-active iodide and searching for localization by electron microscopy and autoradiography, but has been unable to detect selective retention of iodide because apparently it is not securely held in any form in the ciliary processes and washes out during fixation of the tissue.

Optic nerve and glaucoma

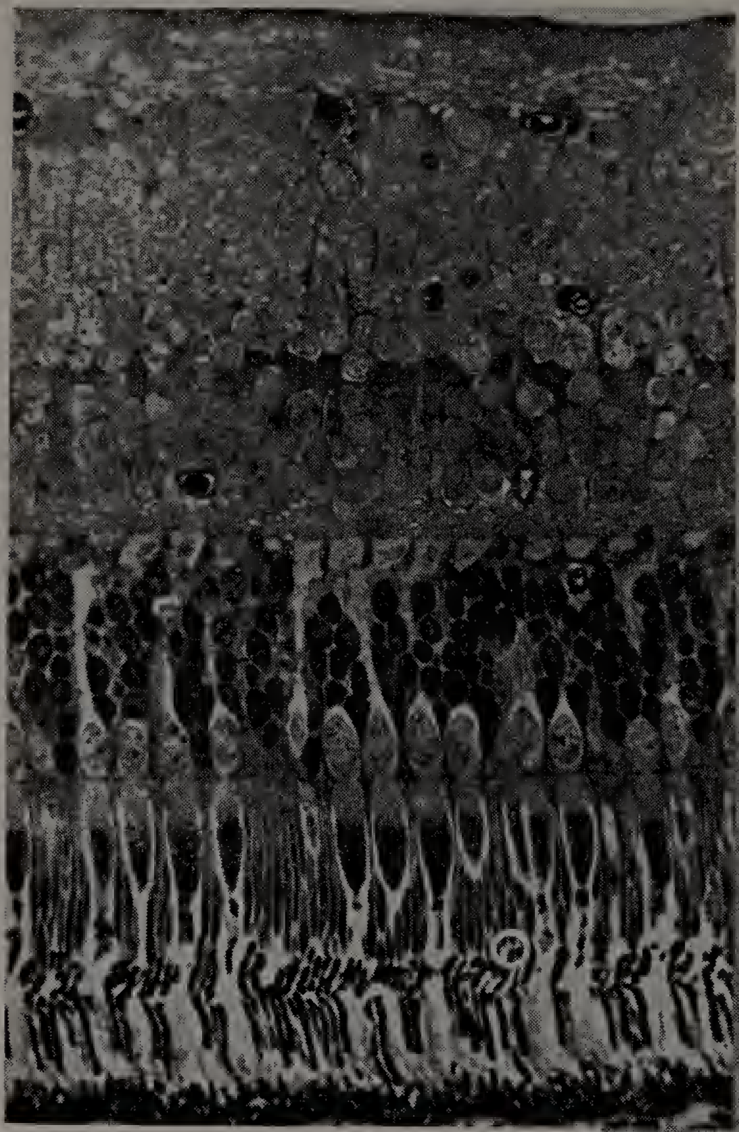
While most effort in research on glaucoma has been put into the study of regulation of the ocular pressure, the ultimate and most crucial problem is understanding, detecting, and averting the effects of abnormally high pressure on the optic nerve. This is a particularly difficult aspect to investigate. However, several new approaches have been made which appear promising. At the fundamental level as to how the optic nerve is injured, techniques for examining the circulation of the nervehead have been explored, through a photodensitometric method by Dr. Meyer, and through fluorescein angiography by Dr. Haining. At the applied clinical level, serial stereo color photos by Dr. Donaldson promise to provide us with the most sensitive means yet devised for detecting slight change in the nervehead, and in time should teach us much about the manner of progression of these changes in patients under treatmeant for glaucoma.

Experimental Pathology

Structure and function of the developing retina

The rat affords a unique opportunity to study the developing retina. While the ultimate structure of the rodent retina is basically similar to that of the human eye, its state of development at birth corresponds to that of the four month human fetus. By two weeks' time on the other hand it has an adult configuration. Thus one can document the changes that occur in a new born rat's retina over a two week period and have an anatomic analog that occurs in the inaccessible human eye over a five months' period.

Drs. Weidman and Kuwabara recorded the electroretinogram daily on new born rats and killed the animals at regular periods for electron microscopy of the eyes. The first sign of rod development occurred at three days. This consisted of elongation of the centrosomes and formation of primordial laminar plates differentiating from smooth endoplasmic reticulum (not from the cell wall as generally believed). The differentation of ganglion cells occurs early but the separation of the outer and inner nuclear layers does not occur until the fifth day when the horizontal cells form synaptic connection with the rod axones. The first indication of an electroretinographic response occurs on the 12th day but within a period



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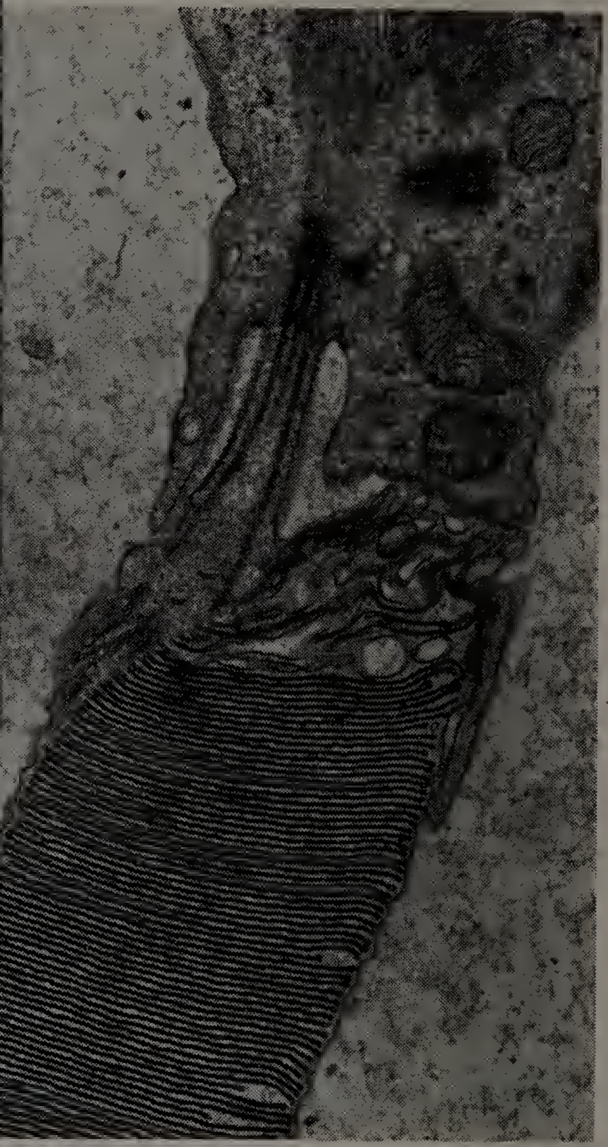
Thin section (0.5μ) of retina as seen with the ordinary microscope. The light-receiving rods and cones (photoreceptors) are at the bottom of the photograph.



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Magnified portion of a photoreceptor as seen with the electron microscope, corresponding to the area indicated by the white circle in the foregoing photograph.

The lower portion of this photograph shows the laminated plates which contain the photosensitive pigment while the upper portion shows the mitochondria which provide the energy for nerve conduction.

Preparations by Dr. T. Kuwabara

of less than 24 hours this response transforms from a just perceptible blip to a mature polyphasic signal.

These are some of the highlights of what is a first attempt to study the entire developing retina. It would be an obtuse person indeed who is not fascinated by the remarkably regular and incredibly intricate sequence of changes that occur in this two weeks' period.

Biochemical embryology of the retina

The chick eye offers a convenient tissue for the study of control mechanisms in the developing retina. Dr. Reif has found that steroid hormones may play a key role in the formation of some of the essential enzymes. Thus steroid hormones can cause the premature induction of glutamotransferase in cultured retinas and hydrocortisone, for example, is necessary for the production of messenger-RNA for this enzyme. Further data have indicated that hydrocortisone may, in fact, be identical with a serum factor previously shown to induce the enzyme. It seems likely that this hormone is responsible, at least in part, for controlling the formation of this protein.

Current studies involve the search for a tissue-culture system not dependent on serum. If successful, such a system would allow investigation of other factors potentially operative in the control of glutamotransferase and associated phenomena. One may expect that studies of this type could eventually add substantial understanding of congenital retinal abnormalities.

Cataracts and the Lens

Biochemistry

Cataracts may be conveniently produced in laboratory animals by feeding galactose or by chemically inducing diabetes. These are the sugar cataracts which have been described in previous reports and appear to be caused by the accumulation of sugar alcohols (sorbitol or dulcitol) in the lens. The early changes may be duplicated in test tubes by incubating rabbit lenses in nutritive solutions rich in galactose.

In a collaborative study with Dr. Winston Barber (Wills Eye Hospital, Phila.), Dr. Kinoshita and Mr. Merola have studied the loss of amino acids and glutathione from these lenses. With the notable exception of lysine and arginine all the amino acids are markedly depressed in lenses exposed to excess galactose for one to two days. A question has been posed whether the loss of the amino acids was due to the swelling of the lens fiber per se or to an obscure metabolic process. The former was found to be the case, for inhibition of the swelling by appropriate adjustments in the osmotic tonicity of the medium bathing the lenses successfully prevented the loss of amino acids.

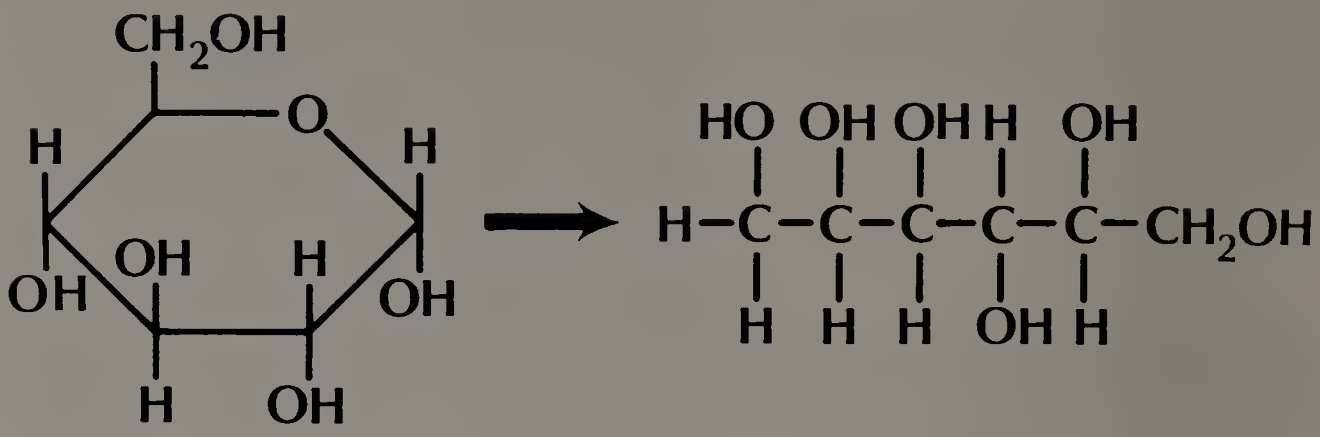

Fig. 2 This conversion of glucose to sorbitol by the aldose reductase in the lens underlies the pathogenesis of cataract formation in diabetes. An analogous process occurs with galactose and constitutes the basis for all sugar cataracts.

Since the enzyme aldose reductase is involved in converting sugars to sugar alcohols it plays a key role in the production of galactose cataract and possibly in diabetic cataract. Considerable effort is therefore being exerted in studying the properties of this enzyme and in searching for inhibitors which may be utilized to control its action. Dr. Jedziniak has purified the enzyme to a considerable degree and found that the enzyme exists in at least two distinct forms which can be separated by their difference in molecular size. The enzymatically active form appears to be protein of relatively low molecular weight. When inactivated either by urea or certain inhibitors the enzyme is converted to protein of higher molecular weight.

Mr. William Holt, a fourth year medical student, devised a starch gel electrophoresis procedure to study the soluble lens proteins. Since this method separates the lens proteins into zones corresponding to alpha, beta, and gamma crystalline it delineates qualitatively the changes occurring in cataract, in aging and other conditions. It was apparent in the study, that beta crystallin is the most complex of the lens proteins in that it is composed of the largest number of protein components. In early stages of cataracts induced in rats by galactose feeding, Mr. Holt found that the changes in the protein patterns affected the rates of migration of only 2 beta zones. All other protein zones remained normal until the cataract progressed to the stage of nuclear opacity. At this stage extensive changes in protein patterns were obvious. The beta and gamma zones showed decrease in staining intensity while the alpha zone became diffuse and spread out. The explanation for these changes remains unknown.

Dr. Chylack has studied cataract formation in the lenses of animals, particularly in relation to diabetes. He has been culturing rabbit lenses according to Dr. Kinoshita's technique, examining the influence of varying glucose concentrations and following changes in the levels of sorbitol and the membrane properties of the lenses. He is setting up methods to extend the period of in vitro culturing of rabbit lenses to two weeks. Also to be studied are the effects of experimental diabetes in animals with varied insulin levels utilizing new diabetogenic substances in preference to standard alloxan.

Effect of antiglaucoma eye drops on the lens

Some evidence has suggested that certain eye drops which have been found most effective in glaucoma treatment could cause disturbances in the lens leading to cataracts. This possibility has been explored in the clinic by Dr. Thoft and in the laboratory by Drs. Michon and Kinoshita. Dr. Thoft's systematic clinical studies have been based on repeated examinations of eyes of glaucomatous patients before and periodically after starting treatment. His findings indicate no significantly deleterious effect on the human lens when the medications are used in the recommended dosages. The laboratory studies are documented under the heading of Toxicology.

Synthetic progestins

The prevalent use of synthetic progestins and estrogens orally for contraception makes it imperative that we obtain information on their possible toxicologic properties. Theoretical considerations suggest an effect on the lens. Dr. Lambert using a technique developed by Dr. Kinoshita for studying the exchange of cations in explanted lenses found that synthetic drugs and natural hormones in this category did indeed cause a considerable increase in permeability of the rabbit lens in vitro with changes in electrolytes, increase in water uptake, and consequent clouding of the lens. Whether or not these changes are sufficient to cause cataracts in life and whether or not they are of practical concern to human beings are aspects currently under investigation.

Neuro-ophthalmology

Cone dysfunction syndrome

Patients presenting with loss of central acuity and of color sensitivity but with no observable abnormality in their fundi are generally suspected of having retrobulbar neuritis or occult disease of the macula. Drs. Zweifach and Ernst Wolfe have collected a group of five patients with acquired cone dysfunction who presented identical clinical symptoms and showed similar responses on dark adaptation, color tests, flicker fields and electroretinography, but who appeared to be specifically distinguished by measurement of variation in visual acuity at different levels of illumination. Whereas patients with retrobulbar neuritis and macular disease characteristically showed a deterioration of vision with lowering of illumination, those with specific cone dysfunction showed an improvement of visual acuity in reduced illumination.

Retinal emboli

We were able this year to make a cinematic record of emboli moving through human retinal vessels. White emboli of an undisclosed nature continually moved along the arteries into the capillary bed and reaggregated in the veins. No source for the emboli was discovered, nor did separate studies of the blood reveal excess fat or white blood cells. The emboli moved in the retinal arteries at an approximate rate of 4 mm/sec but those in the choroidal vessels were immeasurably faster.

Fluorescein angiography

Dr. William Haining (E. B. Dunphy Fellow), Dr. Shirley Wray and photographer Roger Lancaster spent a busy year improving the technique of retinal angiography and amassing a series of clinical records. The procedure consists of injecting a standard bolus of fluorescein into an arm vein and recording its appearance and later disappearance from the retinal and choroidal vessels by a series of photographs taken in rapid succession. Shown up are delays in circulation time, obstructions to the circulation, vessel leaks, or abnormal patterns of the vessels. The Zeiss Fundus Camera has been modified by use of an interference filter system for greater selectivity in the emitted fluorescence and an electro-automatic attachment has been added permitting sequential exposures at 0.6 seconds.

Electroretinography and evoked occipital potentials

Data have been accumulated by Dr. Fricker with his novel technique for electrical measurement of impulses derived from the retina and those derived from the occipital lobes in response to flashes of light. The former indicates predominantly paramacular photoreceptive function whereas the latter represents predominantly macular function. The measurements have clinical usefulness particularly in the presence of opaque ocular media which prevents seeing inside the eye by the usual ophthalmoscopic means. Thus information of prognostic value can be obtained from the electrical signals even in the presence of a dense cataract, and one can differentiate with a fair degree of reliability whether a retina is irreversibly "disorganized" or simply detached.

Pupillary reflexes

A hemikinesimeter is the most recent of a long list of instruments which Dr. Donaldson has developed. This apparatus will permit the testing of pupillary constriction with variable illumination of the two halves of the retina. An identical amount of light enters the pupil at all times but the lighting of a small area on one side is gradually altered to an equivalent illumination on the other half. Scatter in the media is minimized by the focal nature of the light.

The diagnostic value of such a hemikinesimeter is, of course, the differentiation of lesions in the optic tracts from those in the retrogeniculate radiations since the pupillary responses are affected in the former but not in the latter. Ever since Wernicke's observations of the "hemianopic pupil" a century or so ago no apparatus has been found which would reliably overcome the problems of instrumentation. The present apparatus appears to be a considerable improvement over those previously employed.

Retinal immunoglobulins and retinal vascular disease

The recent report in the literature of hypogammaglobulinemia and delayed hypersensitivity in a patient with retinal telangiectasia stimulated Dr. Gordon Johnson to make a study of the sera in patients with Coats' disease (eight patients), Eales' disease (four patients), von Hippel-Lindau's disease (one patient) and solitary retinal angioma (one patient). Immunoelectrophoresis indicated normal values in all these cases.

Infections

Uveitis

To expropriate a sociologic cliché, one might say of uveitis "ye shall always have (it) with you." There is perhaps no more discouraging field in ophthalmology or one in which there are fewer leads. We need help not only from ophthalmologists but from immunologists and from those knowledgeable in the fields of infection and metabolic disease. We most especially need an enclave of people who are versed in all these fields. In the past few years we have had Drs. Elliott, Leibowitz and Martin Flax. Dr. Nesburn and Dr. Langston have included uveitis in their general virologic researches and this past year have made repeated searches for viral or bacterial agents in a variety of obscure cases of intraocular infections. An especial search has been made for mycoplasma (PPL organisms) in the anterior chamber of 20 patients with uveitis but with discouragingly few positive results.

Virology and oncology

Drs. Nesburn and Langston have developed highly sophisticated methods which they have been employing in the study of patients who have unusual and interesting conditions as well as in carrying out extensive studies in experimental animals and tissue culture. Joint studies with the Harvard School of Public Health have been carried out on trachoma and inclusion body diseases. Also related to clinical problems, has been Dr. Nesburn's attempt to grow human malignant eye tumors in tissue culture, with some initial success.

Dr. Nesburn has been exploring oncogenesis (tumor induction) by viruses in experiments in which he has been examining the malignant transformation of rabbit kidney cells in vitro by an adenovirus which has not previously been reported to be oncogenic.

In experimental work in rabbits, Dr. Nesburn has completed a careful systematic characterization of a rabbit herpes virus that is indigenous in some rabbits and is important to recognize and distinguish from human herpes virus in experimental work related to the herpetic dendritic keratitis of human beings. The presence of the rabbit herpes virus if unrecognized can be quite misleading, because it can exist in rabbits without producing symptoms and can be confused with the human virus both by light microscopy and electron microscopy of tissues, being distinguishable only by specific immunologic procedures such as use of specific fluorescent antibodies.

Dr. Nesburn has been examining in tissue culture the mechanism which may be responsible for the growth of the human herpes simplex virus in a typical dendritic form in the living cornea.

Dr. Langston has concentrated in ocular virology. Her most outstanding discovery so far has concerned the localization of the herpes simplex virus in rabbits at the time of acute onset of herpes keratitis. Studies by culture and fluorescein antibody determinations have shown that before the cornea is infected or affected, the virus has already entered the extraocular tissues, principally the lacrimal glands, and from this source the virus is copiously and continuously supplied to the cornea and other structures of the eye, resulting in herpetic keratitis and uveitis. A related study, essentially a sequel, has been carried out in association with Dr. Nesburn concerning recurrence of herpetic keratitis in rabbits, utilizing a strain of virus isolated from a patient with recurrent herpetic keratitis, indicating persistence of virus in the glands to be a critical factor.

Dr. Langston has also evaluated the growth curve of interferon-producing lines of adenovirus-transformed cells and the effect of interferon in treatment of herpes simplex keratitis in rabbits. Interferon was found to be ineffective at the acute stage of the disease, despite claims from Scandinavian clinicians that it is effective against recurrent herpetic keratitis. Differences in the amounts of virus at these different stages may account for the difference in effectiveness found.

An evaluation of a new drug "Anticandida-albicans" showed that in spite of effectiveness in vitro the drug was not effective when applied topically in treatment of candida infection of the cornea in rabbits.

Toxoplasmosis and syphilis

Dr. Gordon Johnson spent most of his six months with us studying the fluorescent test for toxoplasma antibodies in the serum and aqueous humor of patients with uveitis. Early experience with this test, which will be continued by Dr. Johnson in his new post in Toronto, confirms that it is a practical and convenient method with a precise end point.

Dr. Johnson also studied in collaboration with Dr. J. Goldman the cytology of aqueous samples from patients with suspected syphilis. Preparations were made by direct smears on gelatin-coated slides and by smears of centrifuged aqueous but the most satisfactory results were obtained with millipore filters. A promising approach in the future would seem to be the determination of specific immunological sensitivity of these cells to particular antigens.

Toxicology

Research this year in areas of overlap of Toxicology, Pharmacology and Glaucoma have partly been described in the sections on Glaucoma and Cataracts, particularly those aspects involving clinical investigations. Research on toxicology at more basic levels, mainly in the laboratory, has been carried out by Drs. Michon and Lambert.

Dr. Michon, with the guidance of Dr. Kinoshita, has been working on biochemical aspects of ophthalmic pharmacology and toxicology. He has demonstrated the presence of cholinesterase in the lens and has shown that miotic drugs which are under suspicion of causing toxic effects in the lenses of glaucomatous patients have clearly demonstrable effects on animal lenses in tissue culture, causing changes in permeability and appearance of vacuoles.

Dr. Michon has carried out another study with homologs of the anticholinesterase miotic drug demecarium bromide, which have varying chain lengths, demonstrating significant differences in permeability of lens and retina.

Dr. Michon has also been studying the blood retina barrier, and the molecular properties of drugs that influence their penetration of the barrier and their distribution in the retina. He has been employing the anticholinesterase inhibitor echothiophate, and analogs, some polar and some nonpolar, demonstrating striking differences in permeability and in access to the retinal cholinesterase. These observations hold promise of providing better understanding and potentially greater safety with respect to adverse side-effects of drugs on retina and brain.

Dr. Michon in association with Dr. Lambert, has been examining the influence of chlorpromazine on permeability of the lens and formation of diffuse cataract in lenses in tissue culture. This study is part of a comprehensive series of investigations testing a general hypothesis concerning alteration of lens permeability as a common factor in toxicity of drugs to the lens, possibly a mechanism explaining not only some of the toxic effects noted with chlorpromazine and the cholinesterase inhibitors, but also those of the corticosteroids. These investigations have important clinical implications if they can help explain the lens changes induced in patients by a number of widely used drugs.

Dr. Lambert working under the supervision of Dr. Kinoshita, has been principally interested in membrane permeability characteristics, particularly the permeability characteristics of the lens. The influence of progesterone and of estrogens on the rabbit lens has been studied in vitro, using radio-active rubidium in determinations of permeability, active cation transport and cation balance of the lenses.

Also Dr. Lambert has studied the effects of beta and x-irradiation selectively to the front and to the back of the lens in rabbits, producing posterior subcapsular cataracts. After removal of the lenses from the exposed animals he has determined that irradiation can increase the permeability of either the front or the back of the lens, but that active transport and pumping are more efficient anteriorly, compensating for the anterior leakiness, preventing anterior cataract formation, but in the posterior part of the lens pumping is less efficient. Microscopy with the help of Dr. Kuwabara has demonstrated that only the posterior lens fibers swell. Related studies on the influence of phenothiazine drugs on rabbit lenses in vitro are in progress.

Dr. Lambert has carried out studies producing artificial lipid membranes and has examined the influence of ionizing radiations upon them, seeking more fundamental explanations for the manner in which radiation injures the lens. In the artificial lipid membranes he has obtained evidence that radiation injures the lipid, increasing its permeability, and that this is associated with formation of peroxide. Somewhat related work is being carried on utilizing measurements of permeability of artificial lipid membranes to examine effects of progesterone and estrogens.

Miscellaneous Clinical Studies

Although separate from the Howe Laboratory many of the clinical researches performed under the auspices of the Center Grant have had mutual dependence on our core facilities and personnel interaction. Many of these have been described elsewhere and include: Dr. Amoils' development of a cryoprobe for vitreous surgery and present exploration of a self-luminous knife for goniosurgery of glaucoma; Dr. Collis' study of the efficacy of ACTH for treatment of the retrobulbar neuritis of multiple sclerosis; Dr. Meyer's studies on the effect of progestational hormones on the intraocular pressure; Dr. Pruett's study of the chromosomes in patients who have retinoblastoma and in the families of these patients, compared with a control group without retinoblastoma; Dr. Reinecke's studies of temporal arteritis and Dr. Carroll's study of ocular pemphigus; and, Dr. Donaldson's development of photographic techniques including a new model of his anterior segment camera which will have a focal plane shutter making time exposures possible and will permit greater magnification (18 times in the stereo viewer). Except for budgetary purposes there is no clear separation of the clinical researches supported by the Center Grant and the basic researches supported by the Laboratory.

VISION INFORMATION CENTER

We are now in our second year of what we like to think of as an experiment in information retrieval and communication. With the generous support of the National Institute of Neurological Diseases and Blindness and in collaboration with the Countway Library of Harvard Medical School we have concentrated so far firstly on the development of a thesaurus of visual terms that may be fed into a computer and secondly, but simultaneously, on the indexing of article titles that may be automatically retrieved on demand. Forty-nine journals are presently being indexed. We visualize electric typewriter consoles appropriately placed in key universities and hospitals throughout the country connected through the telephone lines with the computer of the Vision Information Center which will give typed responses to requests for the principal recent literature on any subject bearing on vision. We hope to minimize the need for intermediary reference personnel by having easy entrance and exit modes.

This ambitious program is being developed by Dr. Reinecke and a local staff of librarians, Excerpta Medica Foundation, the Harvard Computer Service and a group of working consultants. Conjointly supported by our Center Grant is the computerization of several programmed courses in ophthalmology comprising the first meaningful association of programmed instruction and literature retrieval. Once the initial phases of literature coding and computer accessibility are completed we hope to proceed with the challenging task of applying the developed techniques to the great problems of literature evaluation and information dissemination. The mechanism by which these latter functions will operate remains to be worked out.

TEACHING AND LEARNING

The Howe Laboratory staff participates in teaching at all levels of instruction, giving as well as receiving, of medical students, postgraduate students, residents, visiting staff, and fellow investigators. We blushed immodestly as the Harvard Medical students in open forum declared this past year that the course in ophthalmology, directed by Alfred Scott, was the best in their Introduction to the Clinical Year. We share the satisfaction that comes with Dr. Henry Allen's perennial postgraduate course. We would like to believe the letter of one of our recent residents who wrote, "The quality of intellect, the technical sophistication, and the unassuming spirit impressed me as no school has. It was a marvelous experience for a young man learning an approach to a science while forming his character and goals."

The visiting staff shows its support of the Laboratory in many ways, one of which is evident in the appended list of unsolicited contributors. And the respect in which the Laboratory is held by fellow investigators is evident by the continuingly large number of qualified applicants who would like to join us — and whom we would like to accommodate had we sufficient space.

HONORS AND INVITED LECTURES

Dr. Jin Kinoshita was given an honorary Doctor of Science degree by his alma mater Bard College. Dr. Grant gave the Schoenberg Memorial Lecture on glaucoma. Dr. Cogan gave the deSchweinitz Lecture and was the Invited Guest of the European Ophthalmic Pathology Society. He was also awarded the Howe Medal by the University of Buffalo. Dr. Thomas Weidman was awarded a Ph.D. degree (University of Kansas) with thesis work completed under Dr. Kuwabara's supervision. The collection of historical vignettes prepared by Mr. Charles Snyder was published in book form under the title Our Ophthalmic Heritage. Finally, we have just learned that Dr. Kuwabara is to receive the 1968 Friedenwald Award from the Association for Research in Ophthalmology.

ORGANIZATION AND SUPPORT

The Howe Laboratory has had an administrative framework which, for historical reasons, has been unusual if not unique in medical school curricula. It was founded and initially established at the Harvard Medical School as a separate research department having no official connection with either the Department of Ophthalmology or the Massachusetts Eye and Ear Infirmary. Since 1932 when it came to be housed in the Infirmary it has become progressively allied with the clinical operations of the hospital and has lost, for better or for worse, some of its separate identity. A plaque on the hospital's front entrance, indicating the Laboratory's separate status, was removed long ago and by common consent the Howe Laboratory is recognized as the ophthalmic research division of the Infirmary. A further merging of the two occurred in 1963 when the position of Chief of the Eye Service and Director of the Howe Laboratory were combined into one.*

Certainly the integration of different functions has merit and is the modern way of doing things. In reflecting on accomplishments of the Laboratory, however, one wonders whether or not we may be losing that independence which is essential for basic research and which has afforded a privileged position to the Howe Laboratory in the past.

We are frank to admit that we worry about the incompatibilities of clinical administration and research creativity. Both are tremendously important but require different temperaments and experience. We are not presently in trouble, so far as we are aware, but as both functions grow we want to take precautionary steps before either the clinical or research functions are jeopardized. Accordingly, we have sought means in the past few years to establish a new professorship with a chief responsibility in the area of research. We have, happily, the promise of $300,000 on a matching basis for a Chair and have hopes of interesting another benefactor to complete the necessary endowment during this, the fortieth year of the Laboratory's existence.

The Howe Laboratory has an endowment which although it has been considerably increased in recent years provides only about 10% of the research budget. For the major support we depend on Federal grants, charitable organizations and benevolent individuals who have chosen to invest in eye research through the Howe Laboratory. We are most grateful and reaffirm our intent to do our utmost to merit the faith and sacrifice which these donations represent. We would particularly like to acknowledge the heavy support given our endeavors by the Institute of Neurological Diseases and Blindness, the Atomic Energy Commission, the Massachusetts Lions Eye Research Fund, Inc., Research to Prevent Blindness, Inc., the Genradco Trust, the Shamroth Family Charitable Trust, The Seeing Eye, Inc., and the following list of individuals who have been most generous and thoughtful this past year.

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* Following the period covered by this Annual Report Dr. Cogan resigned as Chief of the Eye Service at the Infirmary to devote more time to Laboratory affairs.

For General Expenses

Individual benefactors
- Anonymous
- Mr. L. A. Angotti
- Dr. Henry F. Allen
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Massachusetts Lions Eye Research Fund, Inc.

Research to Prevent Blindness, Inc.

Shamroth Family Charitable Trust

Max, Martha and Alfred M. Stern Fund

For Specific Projects

American Contract Bridge League Charity Foundation, Corp.
Glaucoma research

The Seeing Eye, Inc.
Ophthalmic Assistants Program

Alfred P. Sloan Foundation
Basic experimental studies in glaucoma

Dr. Francis J. West
Howe Library of Ophthalmology

U.S. Atomic Energy Commission
The carbohydrate metabolism of ocular tissue

U.S. Public Health Service
General Research Support Grant
Center Grant
Ophthalmology Training Grant
Vision Information Center
Pressure regulating mechanisms in glaucoma
Research Career Development Award
Cataracts
Lipid synthesis of non-adipose tissue
Electron microscopy of retinal dehydrogenases
Metabolic histochemistry of the retina

Finally, it is again a pleasure to acknowledge the willing cooperation of the following secretaries, technicians, and others who provided essential supportive services this past year: Inez M. Berry, Rita A. Bregani, Barbara D. Bridgman, Joanne Bruno, Jean M. Caldwell, Marion O. Cameron, Elizabeth E. Colley, Marie Davenport, Frederick M. Dittmar, Kathryn Donaldson, Mary Eichhorn, Cynthia R. Full, Marc B. Garnick, Crista Getz, Jeffrey M. Grant, Susan Hall, Nancy Hardy, Margaret J. Harmon, Barbara Harris, Ellen M. Henson, Cathleen Hoy, Diana Hyams, Robert C. Kasabian, Dixie W. Kaslick, Lawrence W. Kiss, Julia S. Knipp, Brigitta Kreismanis, Alfred Ley, Bonnie A. Parke Lord, Agnes Love, Janis McKittrick, Audrey Melanson, Gloria J. Merola, John Mosher, Werner Mueller, Jr., E. Joann Perkins, David R. Perlo, Peter Poulimenos, Ralph Preston, Mireille Reverdin, Barbara E. Rosenberg, Marjorie E. Saunders, Deborah Sawyer, Jean Segaloff, Laura Strong, Malcolm W. Swan, Gordon Thomas, Bill H. C. Tung, Olga Wehm-Dalton, Dorothy J. White, and Elizabeth M. Whitley.

David G. Cogan, M.D.
Director

HOWE LABORATORY PUBLICATIONS

Brubaker, R. F.

- Determination of episcleral venous pressure in the eye, a comparison of three methods. Arch. Ophthal. 77:110–114, January 1967.
- with Young, L. R.: Noninvasive venous pressure monitoring by the pressure chamber occlusion method. Proc. Conf. Engin. Med. Biol. 20:22.3, November 1967.

Carroll, J. M.

- with Martola, E.-L., Laibson, P. R., and Dohlman, C. H.: The recurrence of herpetic keratitis following idoxuridine therapy. Amer. J. Ophthal. 63: 103–107, January 1967.
- with Miller, D., Holmberg, A., Exford, J., and Boyd, M.: Effect of impression taking on the shape of the cornea in scleral lens fitting. Arch. Ophthal. 78: 331–333, September 1967.

Cogan, D. G.

- Congenital nystagmus. Canad. J. Ophthal. 2: 4–10, January 1967.
- with Kuwabara, T.: The mural cell in perspective. Arch. Ophthal. 78:133–139, August 1967.
- with Kuwabara, T.: Myelin artifacts. Amer. J. Ophthal. 64:622–626, September 1967.
- Editorial: Moonshine, earthshine, and vision. Arch. Ophthal. 78: 695–696, December 1967.
- Extraocular muscles and their diseases. Chapter in *Neuro-ophthalmology Symposium of the University of Miami and the Bascom Palmer Eye Institute*. Vol. III. Ed. by J. L. Smith. St. Louis, Mosby, 1967. 16–34 pp.
- Ophthalmologic problems in diabetes mellitus. Chapter in *Diabetes Mellitus: Diagnosis and Treatment*. Vol. II. Ed. by G. J. Hamwi and T. S. Danowski, New York, American Diabetes Association, Inc. 1967. 191–194 pp.
- with Kuwabara, T.: Retinal Vessels: Anatomy. Proc. XX Internat. Cong. Ophthal., ICS 146:401–409, 1967.

Donaldson, D. D.

- Feature Photos in the Archives of Ophthalmology:
  - Epinephrine pigmentation of the cornea. 78:74–75, July 1967.
  - Free floating cysts. 78:400–402, September 1967.

Grant, W. M.

- with Houle, R. E.: Alcohol, vasopressin and intraocular pressure. Invest. Ophthal. 6:145–154, April 1967.

Haining, W. M.

- with Zweifach, P. H.: Fluorescein angiography in von Hippel-Lindau disease. Arch. Ophthal. 78:475–479, October 1967.

Hørven, I.

- with Hutchinson, B. T.: Exfoliation syndrome: Case reports of 31 and 35 year old patients. Acta Ophthal. 45:294–298, 1967.

Kern, M.

with Leibowitz, H. M., and Elliott, J. H.: Chemotherapeutic immunosuppression of the corneal graft reaction. IV. Systemic corticosteroids. Arch. Ophthal. 78:769–773, December 1967.

Kinoshita, J. H.

with Lou, M. F.: Control of lens glycolysis. Biochem. Biophys. Acta 141:547–559, 1967.

Kupfer, C.

with Downer, J. de C.: Ribonucleic acid content and metabolic activity of lateral geniculate nucleus in monkey following afferent denervation. J. Neurochem. 14:257–263, March 1967.

with Chumbley, L., and Downer, J. de C.: Quantitative histology of optic nerve, optic tract and lateral geniculate nucleus in man. J. Anat. 101:393–401, June 1967.

Kuwabara, T.

with Gorn, R. A.: Retinal damage by visible light. Arch. Ophthal. 77:115–118, January 1967.

Lambert, B. L.

with Kinoshita, J. H.: The effects of ionizing irradiation on lens cation permeability, transport and hydration. Invest. Ophthal. 6:624–634, December 1967.

Langston, D. P.

with Sobin, L. H.: The detection of a viral interfering substance in the Shope papilloma and the VX7 and VX2 carcinomas. J. Exptl. Med. 126:887–897, November 1967.

Leibowitz, H. M.

with Elliott, J. H., and Boruchoff, S. A.: Epithelialization of the anterior chamber following penetrating keratoplasty. Arch. Ophthal. 78:613–617, November 1967.

Michon, J., Jr.

with Kinoshita, J. H.: Cholinesterase in the lens. Arch. Ophthal. 77:804–808, June 1967.

Nesburn, A. B.

Editorial: Progress against rubella. Arch. Ophthal. 77:425–426, April 1967.

with Elliott, J. H., and Leibowitz, H. M.: Spontaneous reactivation of experimental herpes simplex keratitis in rabbits. Arch. Ophthal. 78:523–529, October 1967.

Pruett, R. C.

The effects of local anesthetics upon optic nerve conduction in the cat. Arch. Ophthal. 77:119–123, January 1967.

Horner's syndrome following intra-oral trauma. Arch. Ophthal. 78:420–421, October 1967.

REINECKE, R. D.

with Stephens, K. F.: Quantitative forced duction. Trans. Amer. Acad. Ophthal. Otolaryng. 71:324–329, March–April 1967.

AC:A nomogram. Arch. Ophthal. 77:788, June 1967.

with Herm, R. J.: *Basic Ophthalmology, A Programmed Text. Test Edition.* New York, Appleton-Century-Crofts, 1967. 221 pp.

Programming in ophthalmology, self-instruction in medical education. Chapter in *Proceedings of the Second Rochester Conference, June 24–26, 1965.* Rochester, Rochester Clearinghouse, 1967. 65–74 pp.

SNYDER, C.

Our Ophthalmic Heritage. Boston, Little, Brown and Co., 1967. 170 pp.

WORTHEN, D. M.

with Brubaker, R. F.: A small cataract cryoextractor. Arch. Ophthal. 78:451–454, October 1967.

ZWEIFACH, P. H.

Moving retinal and choroidal emboli. Arch. Ophthal. 78:705–708, December 1967.

HOWE LABORATORY LECTURES

Brubaker, R. F.

Aqueous humor dynamics. Postgraduate Course in Ophthalmology, Harvard Medical School, September 12 and 14, 1967.

Aqueous humor dynamics. Postgraduate Course, Boston University, November 25, 1967.

Cogan, D. G.

Pathology of the optic nerve. 4th Clinical Neuro-ophthalmology Symposium, University of Miami, in Miami, Florida, January 2–6, 1967.

Optic nerve pathology. Boston University Medical Center, February 20, 1967.

Microvascular accidents as seen in the eye. Shattuck Hospital Lecture on Current Neurological Information. I. Cerebral Vascular Disease Symptom Patterns and Treatment, February 27, 1967.

Ocular oscillations. Academy of Ophthalmology, University of Toronto, March 3, 1967.

Conference on Microcirculation as Related to Shock. Department of Biology, Boston University, March 29–April 1, 1967.

Opsoclonus. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 3, 1967.

Symposium: Inborn Metabolic Disease with Associated Ocular Lesions. Irish Ophthalmological Society, in Dublin, Ireland, May 25, 1967.

Metachromatic leucodystrophy. Netherlands Ophthalmological Society, in Rotterdam, the Netherlands, June 6–9, 1967.

Lighting, eye strain and health hazards. Seminar on Performance Criteria for the Luminous Environment. State University Construction Fund, in Saratoga, New York, July 6–7, 1967.

Chairman, Section on Ocular Myopathy. Neuro-ophthalmology Conference, 2nd International Congress in Neurogenetics, in Montreal, Quebec, September 17–23, 1967.

Neuro-ophthalmology. Lecture to the Third Year Class, Harvard Medical School, September 27, 1967.

Neuro-ophthalmology. House Officer Lectures, Massachusetts Eye and Ear Infirmary, June 15 and October 17, 1967.

Neuro-ophthalmology. Postgraduate Course in Ophthalmology, Harvard Medical School, October 20 and 24, 1967.

Ocular oscillations with truncal myoclonus. (Howe Gold Medal Lecture) Buffalo Ophthalmological Club, in Buffalo, New York, November 9, 1967.

The sphingolipidoses and the eye. (The deSchwienitz Lecture) Section on Ophthalmology of the College of Physicians of Philadelphia, in Philadelphia, Pennsylvania, November 16, 1967.

Congenital nystagmus. Wills Eye Hospital, in Philadelphia, Pennsylvania, November 17–18, 1967.

COLLIS, W. J.

with Cohen, D.: The ocular manifestations of rubella in the mentally retarded. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 3, 1967.

Neuroanatomy. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, September–October, 1967.

DONALDSON, D. D.

The eye as an indicator of systemic diseases. Eastern Maine General Hospital, in Bangor, Maine, February 9, 1967.

Foreign bodies in the anterior chamber. Panamanian Ophthalmological Society, in Balboa Heights, Canal Zone, March 16, 1967.

External diseases and neuro-ophthalmology. Series of lectures at the Gorgas Hospital, in Balboa Heights, Canal Zone, March 15–17, 1967.

A binocular direct ophthalmoscope. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 3, 1967.

Clinical manifestations of some uveal tract diseases. New England Ophthalmological Society, April 4, 1967.

Systemic diseases and the eye. University Hospital, in Boston, April 17, 1967.

Lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine:

Neuroanatomy and sensory neuro-ophthalmology. July 18–22, 1967.

Diseases of the anterior segment of the eye. July 24–29, 1967.

Orbital blow-out fractures. House Officer Lecture, Massachusetts Eye and Ear Infirmary, August 5, 1967.

Anterior chamber lesions and iris tumors. Postgraduate Course in Ophthalmology, Harvard Medical School, September 12, 1967.

External diseases of the eye. Series of lectures to the University of Pennsylvania Hospital, in Philadelphia, Pennsylvania, October 9–11, 1967.

Lesions of the anterior chamber angle. Southern Medical Association, in Miami, Florida, November 13–16, 1967.

Orbital floor fractures. New England Ophthalmological Society, December 20, 1967.

FRICKER, S. J.

Clinical application of phase-frequency measurements in ophthalmology. International Conference on Medical and Biological Engineering, in Stockholm, Sweden, August 15, 1967.

Electro-physiology of the visual system. Postgraduate Course in Ophthalmology, Harvard Medical School, September 18, 1967.

GRANT, W. M.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:

Toxicology of the eye, modern interpretations, July 13, 1967.

Systemic drugs and ocular pressure, November 7, 1967.

Drug induced disturbances of vision that may affect driving. American Association for Automotive Medicine, in Philadelphia, Pennsylvania, October 21, 1967.

Systemic drugs and adverse influences on ocular pressure. Drug Symposium of the Council on Drugs, American Academy of Ophthalmology and Otolaryngology, in Chicago, Illinois, October 29, 1967.

Influence of systemic medications on intraocular pressure. Mark J. Schoenberg Memorial Lecture, New York Society for Clinical Ophthalmology and National Society for the Prevention of Blindness, in New York, New York, December 4, 1967.

Glaucoma, gonioscopy and goniotomy. Department of Anesthesiology, Massachusetts Eye and Ear Infirmary, December 6, 1967.

HAINING, W. M.

Interpretation of fluorescein angiography. Cornell Alumni Association, in New York, New York, February 4, 1967.

Fluorescein studies. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 3, 1967.

KINOSHITA, J. H.

Galactose metabolism in the lens. Johnson Foundation, Department of Biophysics and Physical Biochemistry, University of Pennsylvania School of Medicine, in Philadelphia, Pennsylvania, March 16, 1967.

Discussion of paper by Dr. Melvin Freeman, "Lysosomal enzymes associated with vitreous hyalocyte granules." Association for Research in Ophthalmology, in Clearwater, Florida, May 1, 1967.

Lens aldose reductase. Ayerst Laboratories, Biochemistry Division, in Montreal, Quebec, May 24, 1967.

Lens aldose reductase. Conference on Eye Biochemistry, in Woods Hole, June 24, 1967.

Galactose cataracts. House Officer Lecture, Massachusetts Eye and Ear Infirmary, June 27, 1967.

Cataracts in galactosemia. Akita Medical Association, in Akita City, Japan, September 9, 1967.

Cataracts in galactosemia. Department of Ophthalmology, Hirosaki University, in Hirosaki, Japan, September 10, 1967.

Cataracts in galactosemia. Tokyo Ophthalmological Society, in Tokyo, Japan, September 14, 1967.

Cataracts in galactosemia. Lens Biochemistry Discussion Group, in Hakone, Japan, September 16, 1967.

Cataracts in galactosemia. Ophthalmological Society of the Universities of Kyusu, Kurume and Kumamoto, in Fukuoka, Japan, October 8, 1967.

Cataracts in galactosemia. Department of Ophthalmology, Osaka University Medical School, in Osaka, Japan, October 11, 1967.

Cataracts in galactosemia. Department of Ophthalmology, Tottori University, in Yonago, Japan, October 15, 1967.

The effects of galactose on the transport mechanisms of the ocular lens. Transport Colloquia, Western Reserve University School of Medicine, in Cleveland, Ohio, November 30, 1967.

Kuwabara, T.

Fine structure of the retina. Ophthalmology Faculty, Harvard Medical School, January 8, 1967.

Vascular pathology in diabetic retinopathy. New England Deaconess Hospital, February 4, 1967.

Metachromatic substance in the normal human lens. Association for Research in Ophthalmology, in Washington, D.C., March 10, 1967.

Pathology of diabetic retinopathy. Boston University School of Medicine, March 20, 1967.

Retinal synapses. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 3, 1967.

Light damage on the developing retina. Verhoeff Society, in Washington, D. C., April 26, 1967.

Structure of ciliary epithelium. Association for Research in Ophthalmology, in Clearwater, Florida, May 2, 1967.

Retinal vasculature in diabetes and hypertension. Department of Surgery, Yale University School of Medicine, in New Haven, Connecticut, May 12, 1967.

Function of ciliary epithelium. Research Seminar, Department of Ophthalmology, Yale University School of Medicine, in New Haven, Connecticut, May 12, 1967.

Edema of the corneal stroma. 4th Boston Conference on the Cornea, in Andover, Massachusetts, May 27, 1967.

Fine structure of the eye. Series of lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine, July 6–10, 1967.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
  Ciliary epithelium, its fine structure and function, July 11, 1967.
  Ocular electron microscopy, December 26 and 28, 1967.

Lectures to the Department of Anatomy, Harvard Medical School:
  Structure and pathology of the retina, October 20, 1967.
  Retina: Structure and pathology, November 30, 1967.

Light effect to the pigment epithelium. Association for Research in Ophthalmology, in Chicago, Illinois, October 26, 1967.

The retina. Research Seminar, Department of Anatomy, University of Kansas School of Medicine, in Kansas City, Kansas, November 3, 1967.

Electron microscopy — corneal pathology. Cornea Service Seminar, Massachusetts Eye and Ear Infirmary, November 16, 1967.

Fine structure and pathology of the ocular tissue. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, September–December 1967.

Lambert, B. W.

The effect of ionizing radiation on the lens. Association for Research in Ophthalmology, in Clearwater, Florida, May 1, 1967.

Toxic cataracts. Lancaster Courses in Ophthalmology, in Waterville, Maine, July 13, 1967.

The pill and the eye. House Officer Lecture, Massachusetts Eye and Ear Infirmary, December 7, 1967.

Langston, D. P.

Interferon — Its nature and clinical application. House Officer Lecture, Massachusetts Eye and Ear Infirmary, September 12, 1967.

Interferon — Its nature and clinical application. Postgraduate Course in Ophthalmology, Harvard Medical School, October 6, 1967.

Michon, J., Jr.

with Thoft, R. A.: Clinical and laboratory aspects of anticholinesterases. House Officer Lecture, Massachusetts Eye and Ear Infirmary, June 29, 1967.

Ocular cholinesterase. Lancaster Courses in Ophthalmology, in Waterville, Maine, July 14, 1967.

Nesburn, A. B.

Isolation of a rabbit herpes virus. Annual Meeting of the Group in Ocular Microbiology and Immunology, in Gainesville, Florida, April 28, 1967.

Clinical use of antivirals in ophthalmology. Bascom Palmer Eye Institute, in Miami, Florida, April 29, 1967.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
Basic virology, September 12, 1967.
Antiviral substances and the eye, September 14, 1967.

Lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School:
Basic virology, October 4, 1967.
Antiviral substances and the eye, October 11, 1967.

Reinecke, R. D.

Moderator: Conference on Epiphora. New England Ophthalmological Society, January 18, 1967.

Strabismus and AC:A ratio. Egyptian Ophthalmological Society, in Cairo, Egypt, April 4, 1967.

Lacrimal sac implants. Faculty of Medicine Cairo University, in Cairo, Egypt, April 5, 1967.

Viet Nam Ophthalmology:
Brimmer and May School, April 13, 1967.
WEZE Radio, April 20, 1967.
Massachusetts Eye and Ear Infirmary Distaff, July 19, 1967.

Eye care in the Mekong Delta. Volunteers' Dinner Meeting, Massachusetts Eye and Ear Infirmary, May 10, 1967.

Medical problems in Viet Nam. Beth Israel Hospital, May 24, 1967.

Seminar on Viet Nam Medicine. American Medical Association, in Atlantic City, New Jersey, June 18, 1967.

Strabismus and refraction. Lancaster Courses in Ophthalmology, in Waterville, Maine, August 8–12, 1967.

Programming in ophthalmology, self-instruction in medical education. 2nd Rochester Conference, in Rochester, New York, September 15, 1967.

Lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School:
Strabismus, October–November 1967.
Programmed refraction, October 17 and 20, 1967.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
Viet Nam ophthalmology, April 20, 1967.
Dacryocystorhinostomy — Conjunctivo-dacryocystorhinostomy with silicone tubes, October 10, 1967.
Vision Information Center. American Documentation Institute, in New York, New York, October 25, 1967.

SNYDER, C.
Hippocrates the honest. Anesthesia Study Group, Massachusetts Eye and Ear Infirmary, November 8, 1967.
An introduction to the history of ophthalmology. Postgraduate Course in Ophthalmology, Harvard Medical School, November 29, 1967.

WEIDMAN, T. A.
Ultrastructure of developing rat retina. Verhoeff Society, in Washington, D. C., April 26, 1967.
with Kuwabara, T.: Postnatal development of the retina. Symposium on Embryology, Association for Research in Ophthalmology, in Chicago, Illinois, October 27, 1967.

WORTHEN, D. M.
Lens pathology. Postgraduate Course in Ophthalmology, Harvard Medical School, December 5, 1967.

WRAY, S. H.
Fluorescein angiography of the optic disc. Neurological and Neuro-ophthalmological Meeting, Hospital of the University of Pennsylvania, in Philadelphia, Pennsylvania, December 1, 1967.
Papilledema. House Officer Lecture, Massachusetts Eye and Ear Infirmary, December 19, 1967.

ZWEIFACH, P. H.
Nystagmus. House Officer Lecture, Massachusetts Eye and Ear Infirmary, January 24, 1967.
Retinal emboli. Alumni Association of the Massachusetts Eye and Ear Infirmary, April 3, 1967.
Retinal embolism. Von Hippel-Lindau Disease. Cornell Eye Residents Association, in New York, New York, May 2, 1967.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology .... Dollars to be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University, and the income is accredited to the Laboratory.